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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Potter et al. #23  
Serial No. : 09/633,697 Examiner: T.C. McKenzie  
Filed : August 7, 2000 Group Art Unit: 1624  
Confirmation No. 3756  
For : HYDROXYLATION ACTIVATED DRUG RELEASE

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

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Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

In accordance with 37 C.F.R. §1.56 and §1.97(c)(2), Applicants respectfully request that the references relating to the above-identified application listed herein in reverse chronological alphabetical order be considered and made of record in the United States Patent and Trademark Office.

1. Potter GA *et al.*, U.S. Application No. 09/115,016, now U.S. Pub. No. 2002/0037296 published March 28, 2002.

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2. Potter *et al.*, U.S. Pat. No. 6,346,550 B2 issued February 12, 2002.
3. Hoang TTV *et al.*, 2001, "Cytochrome P450 CYP1B1 Expression in Human Cervical Intraepithelial Neoplasia" *British Journal of Cancer* **85**(Suppl 1):78.
4. Potter *et al.*, U.S. Pat. No. 6,214,886 B1 issued April 10, 2001.
5. Stanley LA *et al.*, 2001, "Cytochrome P450 Cyp1b1 In Colon Tumorigenesis" *Drug Metabolism Reviews* **33**(suppl 1):62.
6. Suda Y *et al.*, 2001, "Chemical and biological degradation of 5-fluorouracil prodrugs having high serum albumin binding potencies", *L3 Answer 1 of 1 Chem. Abstract* **119**:62362.
7. Buur A *et al.*, 2001, "Prodrugs of 5-fluorouracil, II. Hydrolysis kinetics, bioactivation, solubility and lipophilicity on N-alkoxycarbonyl derivatives of 5-fluorouracil" *L2 Answer 1 of 1 Chem. Abstract* **102**:12247.
8. Tang YM *et al.*, 2000, "Human CYP1B1 Leu432Val gene polymorphism: ethnic distribution in African-Americans, Caucasians and Chinese; oestradiol hydroxylase activity; and distribution in prostate cancer cases and controls" *Pharmacogenetics* **10**(9):761-766.
9. Potter *et al.*, WO 99/40944 published August 19, 1999.
10. Potter *et al.*, WO 99/40056 published August 12, 1999.
11. Iyer S *et al.*, 1998, "Induction of Apoptosis in Proliferating Human Endothelial Cells by the Tumor-specific Antiangiogenesis Agent Combretastatin A-4" *Cancer Res.* **58**:4510-4514.
12. Ducki S *et al.*, 1998, "Potent Antimitotic and Cell Growth Inhibitory Properties of Substituted Chalcones" *Bioorg. Med. Chem. Letters* **8**(9):1051-1056.
13. Luch A *et al.*, 1998, "Stable Expression of Human Cytochrome P450 1B1 in V79 Chinese Hamster Cells and Metabolically Catalyzed DNA Adduct Formation of Dibenzo[ $\alpha,1$ ]pyrene" *Chem. Res. Toxicol.* **11**:686-695.
14. Murray GI *et al.*, 1998, "Enhanced expression of cytochrome P450 in stomach cancer" *Br J Cancer* **77**(7):1040-1044.
15. Ohsumi K *et al.*, 1998, XP-002102895, "Novel Combretastatin Analogues Effective against Murine Solid Tumors: Design and Structure – Activity Relationships" *J. Med. Chem.* **41**(16):3022-3032.
16. Dark GG *et al.*, 1997, "Combretastatin A-4, an Agent That Displays Potent and Selective Toxicity toward Tumor Vasculature" *Cancer Res.* **57**:1829-1834.
17. Hiromitsu S, 1996, JP 08188546, (Patent Abstracts of Japan).

18. Pettit GR *et al.*, 1995, "Antineoplastic agents 322. Synthesis of combretastatin A-4 prodrugs" *Anti-Cancer Drug Design* **10**:299-309.
19. Tully W *et al.*, 1995, "Preparation of cyclomanganated chalcones and their reactions with methyl acrylate and other  $\alpha,\beta$ -unsaturated carbonyl compounds" *J. Organometallic Chem.* **503**(1):75-92.
20. Cushman *et al.*, U.S. Pat. No. 5,430,062 issued July 4, 1995.
21. Bosslet K *et al.*, CA Pat. No. 2,109,259 issued April 28, 1994.
22. Satoh *et al.*, U.S. Pat. No. 5,276,058 issued January 4, 1994.
23. Klein E, 1994, Chemical Abstracts "Cosmetic compositions containing chalone derivatives" *Am. Chem. Soc.* **120**(1):422 (Abstract 14,657c).
24. Won CM, 1994, "Kinetics and mechanisms of hydrolysis of tyrphostins" *Intl. J. Pharmaceutics* **104**:29-40.
25. Cushman M *et al.*, 1992, XP-000571677, "Synthesis and Evaluation of Analogues of (Z)-1-(4-Methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)ethene as Potential Cytotoxic and Antimitotic Agents" *J. Med. Chem.* **35**(12):2293-2306.
26. Doehmer J *et al.*, 1991, "Chinese Hamster Cells Genetically Engineered for Stable Expression of Cytochromes P450" *Meth. Enzymol.* **206**:117-122.
27. Hussoin S *et al.*, 1991, XP-002102894, "Polyhydroxylated Phenylacrylic Acid Derivatives as New Anti-tumor Agents" *J. Pharmaceut. Sci.* **80**(5):416-418.
28. Levitzki A *et al.*, EP 0 322 738 A2 published May 7, 1989.
29. Barrie *et al.*, 1989, "Inhibition of 17 $\alpha$ -Hydroxylase/C17-C20 Lyase By Bifluranol And Its Analogues" *J. Steroid Biochem.* **33**(6):1191-1195.
30. Pamer EG *et al.*, 1989, "Identification of a developmentally regulated cysteine protease of *Trypanosoma brucei*" *Mol. and Biochem. Parasitology* **33**:27-32.
31. Carmichael J *et al.*, 1987, "Evaluation of a Tetrazolium-based Semiautomated Colorimetric Assay: Assessment of Chemosensitivity Testing" *Cancer Res.* **47**:936-942.
32. Eckert H *et al.*, 1987, "Triphosgene, a Crystalline Phosgene Substitute" *Agnew, Chem. Int. Ed. Engl.* **26**(9):894-895.
33. Akihiko W, 1986 JP 61076433, (Patent Abstracts of Japan).

34. Burke MD et al., 1985, "Ethoxy-, pentoxy- and benzyloxyphenoazones and homologues: a series of substrates to distinguish between different induced cytochromes P-450" *Biochem Pharmacol* 34(18):3337-3345.
35. Kazuo K et al., JP 56016474 published February 17, 1981.
36. Amble E et al., 1979 "Formation of 2-Oxazolidinones from N-Benzylloxycarbonyl-2,2'-dichlorodiethylamine; Demonstration of Chloride Catalysis" *Acta Chem. Scand.* 33(8):584-586.
37. 1978, "I.26 Fractional Distillation At Atmospheric Pressure" *Vogels Textbook of Practical Organic Chemistry*, 4th Ed. 878:146-155.
38. McMurray JE et al., 1974, "A new method for the reductive coupling of carbonyls to olefins: synthesis of  $\beta$ -carotene" *J. Am. Chem. Soc.* 96(14):4708-9.
39. Wittig G, et al., 1973, "Methylenecyclohexane" *Org. Synth. Coll.* 5:751-754.
40. Pappalardo G et al., 1968, XP-002102896, "Relation between structure and antibacterial action of arylthioamides, II. Antibacterial activity, ultraviolet and infrared spectra, and acid hydrolysis of aryl- and arylvinylthioamides" page 2014; see *abstract & Farmco, et. Sci.* 22(10):808-820 (1967) [*Chemical Abstracts* 68(5):21141r].
41. Gutsche CD et al., 1959, Chemical Abstracts, "Experiments in the colchicine field" *Am. Chem. Soc.* 53(9):9122-9126.

The cited documents are listed in the accompanying PTO Form 1449. Copies of the documents are submitted herewith in one bound volume. Applicants also enclose an English abstract of document 33 as published at <http://ep.espacenet.com>.

Identification of the documents listed in the attached PTO Form 1449 is not to be construed as an admission of Applicants or Attorneys for Applicants that such documents are available as "prior art" against the above-identified application.

Applicants enclose herewith the fee required pursuant to 37 C.F.R. §1.17(p).

Applicants do not believe that any additional fee is required with this submission. Nevertheless, any required fees not enclosed herewith may be charged to Deposit Account No. 02-4377. Two copies of this page are enclosed.

Respectfully submitted,

Dated: February 19, 2003



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Enclosures